minocycline activity per milliliter (estimated). Use this solution within 3 hours of preparation.

(ii) *Calculations—(a)* Calculate the minocycline content of the single-dose vial as follows:

$$\text{Milligrams of minocycline per single-dose vial} = \frac{A_u \times P_s \times d}{A_s \times 1{,}000}$$

where:

A_u= Area of the minocycline peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);

A_s= Area of the minocycline peak in the chromatogram of the minocycline working standard:

P_s= Minocycline activity in the minocycline working standard solution in micrograms per milliliter; and

d = Dilution factor of the sample.

(*b*) Calculate the minocycline content of the multiple-dose vial as follows:

$$\text{Milligrams of minocycline per multiple-dose vial} = \frac{A_u \times P_s \times d}{A_s \times 1{,}000 \times n}$$

where:

A_u= Area of the minocycline peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);

A_s= Area of the minocycline peak in the chromatogram of the minocycline working standard:

P_s= Minocycline activity in the minocycline working standard solution in micrograms per milliliter;

d = Dilution factor of the sample.

n = Volume of sample solution assayed.

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in § 436.32(b) of this chapter, using a solution containing 5 milligrams per milliliter.

(4) [Reserved]

(5) *Depressor substances.* Proceed as directed in § 436.35 of this chapter.

(6) *Moisture.* Proceed as directed in § 436.201 of this chapter, using the sample preparation described in paragraph (d)(4) of that section.

(7) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 10 milligrams of minocycline per milliliter.

[39 FR 19076, May 30, 1974, as amended at 43 FR 11166, Mar. 17, 1978; 43 FR 34457, Aug. 4, 1978; 44 FR 22058, Apr. 13, 1979; 46 FR 60568, Dec. 11, 1981; 50 FR 19920, May 13, 1985; 53 FR 32609, Aug. 26, 1988; 54 FR 47205, Nov. 13, 1989]

§ 446.265 Oxytetracycline injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Oxytetracycline injection is a solution of oxytetracycline with or without one or more suitable and harmless buffer substances, anesthetics, preservatives, antioxidants, complexing agents, and solvents. Each milliliter contains 50 milligrams or 125 milligrams of oxytetracycline. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of oxytetracycline that it is represented to contain. It is sterile. It is nonpyrogenic. It contains no depressor substances. Its pH is not less than 8.0 and not more than 9.0. The oxytetracycline used conforms to the standards prescribed by § 446.65a(a)(1), except sterility, pyrogens, and depressor substances.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The oxytetracycline used in making the batch for potency, moisture, pH, absorptivity, identity, and crystallinity.

(*b*) The batch for potency, sterility, pyrogens, depressor substances, and pH.

(ii) Samples required:

(*a*) The oxytetracycline used in making the batch: 10 packages, each containing approximately 300 milligrams.

(*b*) The batch:

(*1*) For all tests except sterility: A minimum of 10 immediate containers.

(2) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.106 of this chapter, preparing the sample for

assay as follows: Transfer an accurately measured representative quantity of the sample to an appropriate-sized volumetric flask. Dilute to volume with 0.1*N* hydrochloric acid to obtain a stock solution of convenient concentration containing not less than 150 micrograms of oxytetracycline per milliliter (estimated). Further dilute an aliquot of the stock solution with sterile distilled water to the reference concentration of 0.24 microgram of oxytetracycline per milliliter (estimated).

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in § 436.32(b) of this chapter, using a solution containing 5.0 milligrams of oxytetracycline per milliliter.

(4) [Reserved]

(5) *Depressor substances.* Proceed as directed in § 436.35 of this chapter.

(6) *pH.* Proceed as directed in § 436.202 of this chapter, using the undiluted solution.

[43 FR 11166, Mar. 17, 1978, as amended at 46 FR 60568, Dec. 11, 1981; 48 FR 51293, Nov. 8, 1983; 50 FR 19920, May 13, 1985]

§ 446.267 Oxytetracycline hydrochloride for injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Oxytetracycline hydrochloride for injection is a dry mixture of oxytetracycline hydrochloride and a suitable buffer substance. Its potency is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of oxytetracycline that it is represented to contain. It is sterile. It is nonpyrogenic. It contains no depressor substances. Its loss on drying is not more than 3.0 percent. Its pH in an aqueous solution containing 25 milligrams per milliliter is not less than 1.8 and not more than 2.8. The oxytetracycline hydrochloride used conforms to the standards prescribed by § 446.67a(a)(1), except sterility, pyrogens, and depressor substances.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The oxytetracycline hydrochloride used in making the batch for potency, loss on drying, pH, absorptivity, identity, and crystallinity.

(*b*) The batch for potency, sterility, pyrogens, depressor substances, loss on drying, and pH.

(ii) Samples required:

(*a*) The oxytetracycline hydrochloride used in making the batch: 10 packages, each containing approximately 300 milligrams.

(*b*) The batch:

(*1*) For all tests except sterility: A minimum of 10 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Reconstitute as directed in the labeling. Then, using a suitable hypodermic needle and syringe, promptly remove all the withdrawable contents if it is represented as a single dose container; or, if the labeling specifies the amount of potency in a given volume of the resultant preparation, remove an accurately measured representative portion from the container. Dilute the sample thus obtained with sufficient 0.1*N* hydrochloric acid to obtain a stock solution of convenient concentration containing not less than 150 micrograms of oxytetracycline per milliliter (estimated). Further dilute an aliquot of the stock solution with sterile distilled water to the reference concentration of 0.24 microgram of oxytetracycline per milliliter (estimated).

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section, except use diluting fluid D in lieu of diluting fluid A.

(3) *Pyrogens.* Proceed as directed in 436.32(b) of this chapter, using a solution containing 5.0 milligrams per milliliter.

(4) [Reserved]

(5) *Depressor substances.* Proceed as directed in § 436.35 of this chapter,